REMARKS

Claims 1 and 3 – 10 and 26 are currently pending and under examination, with Claims 11 – 25 having been withdrawn from consideration. In the Office Action, Claims 1 – 10 were rejected under Section 103 as allegedly obvious from the disclosure in U.S. Patent No. 4,784,173 to Nelson et al. ("Nelson" or "Nelson '173").

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration and allowance of all claims is requested in view of the above amendments and following remarks.

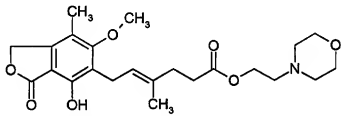
The present claims relate to a process for treatment of mycophenolate mofetil of formula I contained in a reaction product together with a dimer thereof as a by-product impurity. The process comprises, among other things, contacting the reaction product containing the mycophenolate mofetil of formula I and dimer by-product impurity thereof with a primary or secondary amine to make a reaction product mixture and to cause dimer in the mixture to be converted into one or more monomer amide derivatives of mycophenolic acid in the reaction product mixture, and then recovering mycophenolate mofetil from the reaction product, wherein the mofetil recovered from the reaction product mixture contains a substantially reduced dimer by-product impurity component.

As Applicants pointed out in their previous response, Nelson '173 does not ever refer to the existence of any dimer by-product of a mycophenolate mofetil of formula I in a reaction product. Consequently, Nelson '173 cannot reasonably be said to have taught or suggested to a person of skill in the art, who had no knowledge of Applicants' invention, a way of teating a reaction product containing a mycophenolate mofetil according to formula I and dimer by-product impurities thereof for the purpose of enabling recovery of the mycophenolate mofetil from the reaction mixture with a substantially reduced amount of dimer by-product impurities. For one thing, it has not been shown that Nelson '173 was even dealing with a mycophenolate mofetil according to formula I of Claim 1. In fact, as explained in more detail below, the Formula I composition disclosed in Nelson '173 does not even encompass in its scope the formula I mycophenolate mofetil material to which claim 1 is directed. So Nelson '173 was not even dealing with the same material specified in Applicants' claims and, as a result, Nelson '173 cannot be said to have suggested a way of treating a reaction product containing the mycophenolate mofetil of formula I and associated dimer impurities in accordance with Applicants' Claim 1 process.

Again, no part of Nelson '173 has been shown to refer to or suggest treatment of a reaction product containing the formula I mofetil and associated dimer impurities using an amine in order to provide a reaction product mixture with a substantially reduced dimer content, and from which a substantially purified mycophenolate mofetil product can be recovered. The mention in Nelson '173 of an amine treatment is said to be for converting a Formula E derivative of mycophenoloic acid to a certain Formula I heterocyclic aminoalkyl esters of mycophenoloic acid. This has nothing whatsoever to do with treatment of a reaction product containg the formula I mycophenolate mofetil/ dimer impurities as called for in Claim 1, and would not have led a person of skill to such a process.

Nonetheless, the Examiner continues to cite Nelson '173, apparently contending that even if mycophenolate dimers are not explicitly mentioned in Nelson, they nonetheless must have been inherently present because, in her view, Nelson '173 is using the same process to make the same material. With respect, this is a conjectural assertion unsupported by the actual disclosure of Nelson '173, which limits the disclosed esters of mycophenolic acid to compounds which do not include those to which the present claims are directed. As discussed below, Nelson '173's Formula I definitions do not allow for Z = hydrogen, which is the case with Applicants' formula I compound to which Claim 1 is directed.

To better clarify the many key differences between the present invention and what is described in Nelson '173, Applicants have further amended Claim 1 to specify a process for the treatment of the following mycophenolate mofetil of formula I contained in a reaction product, which includes this mycophenolate mofetil compound together with one or more dimer by-products as impurities:



The reaction product containing this compound is contacted with a primary or secondary amine to cause formation of a reaction product mixture in which the aforesaid dimer impurity is converted to one or more monomeric amide derivatives of mycophenolic acid in the reaction product mixture, such as by cleavage of the dimer or some other divisive reaction. The

mycophenolate mofetil is recovered from the reaction product mixture with a substantially lower amount of dimer by-product impurities.

This is not disclosed or suggested in Nelson '173. Again, Nelson '173 fails to disclose the mycophenolate mofetil compound of formula I to which Claim 1 is directed. The Examiner never specifically says which of the compounds of the '173 patent she believes corresponds to the "mycophenolate mofetil" of formula I of the present invention; however, it seems she may be referring to Nelson's Formula I, defined at Col. 3, lines 1 – 58, since that is the formula Nelson '173 says results from treatment with the amine of Formula F at Col. 10.

However, according to the definition of Nelson's Formula I, it is apparent that, among other things, the "Z" variable in Nelson's Formula would have to be hydrogen in order for this formula to correspond to the mycophenolate mofetil formula I specified in the present claims. This is not allowed, however. Nelson '173 defines only four possibilities for the "Z" variable, (a) – (d), in its Formula I compounds; but none of these variables allows for the "Z" to be hydrogen. See, Col. 3, lines 12-50, of the '173 patent. Thus, Nelson's Formula I plainly is not the same as the mycophenolate mofetil compound of formula I to which the present claims are directed and, as a result, Nelson '173 cannot be said to have suggested carrying out any process on a reaction product containing the formula I compounds of Claim 1.

Alternatively, the Examiner "might" be referring to Nelson's Formula II, (defined at Col. 3, lines 60 – 68). However, it is equally apparent that compounds according to Formula II of Nelson also do not correspond to the mycophenolate mofetil compound of formula I to which the present claims are directed.

In particular, in Nelson's Formula II, it is evident the "Y^1" variable would have to be -$(CH_2)_2$-O-$(CH_2)_2$- and the "m" variable would have to be "two" in order for this Formula to encompass the mycophenolate mofetil for formula I specified in the present claims. However, the structure of formula I in Applicants' claims is not encompassed by the definition of Formula II in Nelson '173. At Col. 4, lines 10 & 11, Nelson states that "when m is two, the Y^1 does not include -$(CH_2)_2$-O-$(CH_2)_2$- ." Accordingly, the formula I structure of Claim 1 is also not encompassed within Nelson's Formula II.

Another reason Formula II of Nelson '173 cannot be said to correspond to the mofetil compound of formula I to which the claimed invention is directed is the proviso in Nelson '173 vis-à-vis Formula II (detailed at Column 4, lines 5-6) that Y^1 must be a "lower alkylene

structure." In this regard, the mycophenolate mofetil of formula I of Claim 1 contains an oxacycloalkane structure, which is plainly not a "lower alkylene" structure as required in Nelson's Formula II compounds.

The same point of distinction holds true for Formula I of Nelson '173 due to the proviso at lines 51-53 of Col. 3 that the "Y" structure must be lower alkylenic, as defined. However, as pointed out above, the ring structure on the right-hand end of the mycophenolate mofetil of formula I of Claim 1 is an oxacycloalkane structure, with no unsaturation in any carbon-carbon bonds. The right-hand ring structure of the formula I compound of Claim 1 is very plainly not lower alkylenic, as required by Formula I of Nelson '173.

Hence, it is apparent that Nelson '173 is directed to processes that make derivatives of mycophenolic acid which are not the same as the formula I mycophenolate mofetil to which Claim 1 is directed. Since Nelson '173 has not been shown to disclose the mycophenolate mofetil of formula I specified in Applicants' claims, it follows that Nelson cannot reasonably be said to disclose or suggest a process that would have been useful for treating a reaction product containing the formula I compound and dimer impurities thereof addressed in accordance with the presently claimed process.

Beyond the structural differences in the mycophenic acid derivatives, etc. of Nelson '173 and the mycophenolate mofetil of formula I of Applicant's claims, it is noted that Claim 1 of the present application also calls for separation of the mycophenolate mofetil of formula I from the dimer by-products (i.e., purified) by treating the reaction product with a primary or secondary amine. The formula I mofetil is then recovered from the resulting material with a substantially lower dimer content. While Nelson '173 may use the word "purification," the portion of the disclosure of Nelson '173 referred to by the Examiner as disclosing "purification" has not been shown to teach or suggest application of an amine to a reaction product containing materials the same or even similar to those treated by the process claimed in the present case. In fact, the "purification" methodology mentioned in Nelson at Col. 10, lines 25-34, bears no relation at all to the treatment called for in Applicants' claims. Nelson's so-called "purification" is said to be carried out by "filtration, extraction, crystallization, ... or a combination of the procedures." There is no mention of "purifying" the product by a chemical or other treatment bearing any similarity whatsoever to what Applicants call for in their claims.

Nelson '173's use of an "amine" is described only in terms of what is said to be conversion of mycophenolic acid derivative compounds according to Formula E to compounds

according to Nelson '173's Formula I. As mentioned above, Formula I of Nelson '173 is not the same as the mofetil formula I compound to which the present claims are directed. And Nelson '173's use of an amine to convert Formula E mycophenolic acid derivatives has nothing whatsoever to do with purification of a reaction product containing the claimed mycophenolate mofetil formula I compound and associated dimer by-products thereof, much less ridding any such reaction product of its "dimer" component.

Thus, Nelson '173 cannot lawfully be said to anticipate or suggest the claims of the present case because, among other things, the mofetil formula I material with which the present claims are concerned has not been shown to be the same as the Formula I/II material described in Nelson '173. Hence the Examiner cannot lawfully reject Applicants' claims on the ground that the claims would "inherently" be practicing what is described in Nelson '173, or that Nelson '173 would have suggested to a person of skill the practice of the method claimed by Applicants.

Moreover, it has not been shown how Nelson '173 could be said to describe or to have suggested use of an amine compound, as claimed, to treat a reaction product containing a mycophenolate mofetil according to formula I of Applicant's claims for cleaving or otherwise breaking down dimer impurities within the reaction product because, among other things, Nelson '173 only describes use of an amine material to convert what is said to be an "activated carbonyl or thiocarbonyl derivative" of a certain Formula E material shown and defined at Col. 9, lines 51-65 of Nelson '173) to a compound according to the Formula I compound of Nelson '173. As described above, the so-called "activated carbonyl or thiocarbonyl derivative" of Formula E is NOT disclosed to be a dimer of any kind, much less one according to formula II shown on page 2 of Applicants' published '134 PCT application, nor is there any evidence whatsoever that such a dimer compound would "inherently" have been present (or would have been known by a person of skill to be present) as part of these so-called activated carbonyl or thiocarbonyl "derivatives" of Formula E of Nelson '173.

Having failed to show by competent evidence that Applicants' claims would have been inherently practiced by one of ordinary skill who followed the teachings of Nelson '173, the Examiner simply has not made out a lawful basis upon which to reject Applicants' claims under Section 102. Given this, it is even more apparent that the disclosure of Nelson '173 cannot reasonably be said to have "suggested" the subject matter called for in Applicants' claims to a person of ordinary skill in the art. The only mention in Nelson '173 of "purification" is a perfunctory reference at Col. 8, lines 13-14 that certain "end product(s)" may be "purified by

conventional procedures." So, not only does Nelson '173 fail to suggest the presence of any dimer "impurities" of a formula I mycophenolate mofetil in a reaction product mixture, but there is also no suggestion in Nelson '173 of "purification" of any such reaction product by treatment of the same with an amine as required by Applicants' claims.

Again, it has it been shown that any reaction product mixture made according to Nelson '173 would contain any dimer impurity material as called for in Applicants' claims, or that a person of ordinary skill would have expected any such material to be present. In fact, Applicants have affirmatively shown the contrary, i.e., that the materials to which their claims are directed would not have been expected to be included in any of those substances made or present in any material treated by an amine compound according to Nelson '173's procedures. Thus, while Applicants have affirmatively shown that no prima facie case of "inherent" or any other form of anticipation has been made out, they have also demonstrated beyond question that what they claim would not have "inherently" been practiced by one who followed the teachings of Nelson'173. It therefore follows, a priori, that Nelson'173 would not have suggested the subject matter of Application to a person of ordinary skill in the art.

In light of the foregoing, the present application is believed to be in condition for allowance and entry of the foregoing amendments and allowance of all pending claims is respectfully solicited.

In the event this response is not timely filed, Applicants hereby petition for whatever extension of time is needed to cause the same to be filed in a timely manner. Any fee required for this extension, along with any other fees which may be due with respect to this submission, may be charged to our Deposit Account No. **12-2355**.

Respectfully submitted,
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Date: May 10, 2011
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